

In the claims:

1. A composition comprising HIV proteins isolated from a lysate of an HIV isolate which has been treated to remove human HLA class I and class II antigens present in said lysate, wherein said proteins have been  
5 deglycosylated and wherein said proteins comprise at least one epitope region which does not elicit an immune response in man when encountered by infection or environmental exposure but does elicit an immune response in at least one non-human mammalian species.
2. A composition in accordance with claim 1, wherein said epitope region encompasses a neutralizing or inactivating region of said HIV protein.
3. A composition in accordance with claim 1, wherein said epitope region has an amino acid sequence which corresponds to or immunologically mimics a portion of a human protein amino acid sequence.
4. A composition in accordance with claim 1, which has been enriched for said epitope region(s).
5. A composition in accordance with claim 4, wherein said epitope region(s) comprises at least about 25% of said protein.
6. A composition in accordance with claim 5, wherein said epitope region(s) comprises between about 50% and about 95% of said protein.
7. A composition in accordance with claim 1, which comprises a mixture of lysates from different HIV isolates.
8. A composition in accordance with claim 1, which comprises a mixture of lysates from HIV<sub>1MN</sub>, HIV<sub>1BAL</sub>, and HIV<sub>2NZ</sub>.
9. A composition in accordance with claim 1, wherein said epitope region corresponds to or mimics at least one epitope region of proteins of HIV isolate

5 HIV1<sub>sf2</sub> which does not elicit an immune response in man when encountered by infection or environmental exposure but does elicit an immune response in at least one other mammalian species.

10. A composition in accordance with claim 9, wherein said epitope region corresponds to or mimics an epitope region of at least one of the following HIV1<sub>sf2</sub> proteins:

- 5 (a) envelope gp120 external glycoprotein;  
(b) envelope gp41 transmembrane glycoprotein;  
(c) reverse transcriptase;  
(d) protease p10; or  
(e) gag precursor.

11. A composition in accordance with claim 10, wherein at least one of said epitope regions of HIV<sub>sf2</sub> proteins comprises:

- 5 (a) a region extending from amino acid residue 4 through amino acid residue 27 of gp120 glycoprotein;  
(b) a region extending from amino acid residue 54 through amino acid residue 76 of gp120 glycoprotein;  
10 (c) a region extending from amino acid residue 502 through amino acid residue 541 of gp41 transmembrane glycoprotein;  
(d) a region extending from amino acid residue 254 through amino acid residue 295 of reverse  
15 transcriptase heterodimer p66/55;  
(e) a region extending from amino acid residue 69 through 94 of protease p10;  
(f) a region extending from amino acid residue 166 through amino acid residue 181 of gag gene protein  
20 p24;

- 25 (g) a region extending from amino acid residue 390 through amino acid residue 410 and amino acid residue 438 through 443 of gag gene protein p7;
- (h) a region extending from amino acid residue 2 through amino acid residue 23 of gag gene protein p17; or
- (i) a region extending from amino acid residue 89 through amino acid residue 122 of gag gene protein p17.

12. A composition in accordance with claim 1, which further comprises an adjuvant.

13. A composition in accordance with claim 12, wherein said adjuvant comprises a carrier molecule to which the HIV protein is coupled.

14. A composition in accordance with claim 13, wherein said carrier molecule comprises poly-L-lysine, keyhole limpet hemocyanin, thyroglobulin, an albumin or tetanus toxoid.

15. A composition in accordance with claim 13, wherein said carrier molecule comprises multiple repeats of a glycopeptide.

16. A composition in accordance with claim 15, wherein said carrier molecule comprises multiple repeats of muramyl dipeptide.

17. A composition in accordance with claim 16, wherein said multiple repeats of muramyl dipeptide are crosslinked.

18. A composition in accordance with claim 17, wherein said multiple repeats of muramyl dipeptide comprise a terminal dipeptide of L-alanine-D-isoglutamine.

19. A composition comprising a synthetic peptide which comprises an epitope region which corresponds to or mimics a neutralizing or inactivating region of an HIV protein, wherein said peptide does not elicit an

immune response in humans when encountered by infection or environmental exposure but does elicit an immune response in at least one non-human mammalian species.

20. A composition in accordance with claim 19, wherein said epitope region has an amino acid sequence which corresponds to or mimics a portion of a human protein.

21. A composition in accordance with claim 19, wherein at least one amino acid within said epitope region is modified to enhance MHC interactions or the immune response obtained following administration of said peptide to a non-human mammal.

22. A composition in accordance with claim 21, wherein at least one amino acid is modified so as to create an amphipathic helix with said epitope region bracketed between hydrophilic amino acids and hydrophobic amino acids.

23. A composition in accordance with claim 19, comprising a mixture of said synthetic peptides, wherein said peptides comprise epitope regions which correspond to or mimic more than one neutralizing or inactivating region of HIV proteins.

24. A composition in accordance with claim 19, wherein said epitope region corresponds to or mimics a neutralizing or inactivating region of a protein of HIV isolate HIV1<sub>SF2</sub>.

25. A composition in accordance with claim 23, wherein said epitope regions correspond to or mimic more than one neutralizing or inactivating region of proteins of HIV isolate HIV1<sub>SF2</sub>.

26. A composition in accordance with claim 24 or 25, wherein said HIV1<sub>SF2</sub> protein comprises:

- (a) envelope gp120 external glycoprotein;
- (b) envelope gp41 transmembrane glycoprotein;

(c) reverse transcriptase;

(d) protease p10; or

(e) gag precursor.

27. A composition in accordance with claim 26, wherein said neutralizing or inactivating region of HIV<sub>SF2</sub> protein comprises:

- 5 (a) a region extending from amino acid residue 4 through amino acid residue 27 of gp120 glycoprotein;
- (b) a region extending from amino acid residue 54 through amino acid residue 76 of gp120 glycoprotein;
- 10 (c) a region extending from amino acid residue 502 through amino acid residue 541 of gp41 transmembrane glycoprotein;
- (d) a region extending from amino acid residue 254 through amino acid residue 295 of reverse transcriptase heterodimer p66/55;
- 15 (e) a region extending from amino acid residue 69 through 94 of protease p10;
- (f) a region extending from amino acid residue 166 through amino acid residue 181 of gag gene protein p24;
- 20 (g) a region extending from amino acid residue 390 through amino acid residue 410 and amino acid residue 438 through 443 of gag gene protein p7;
- (h) a region extending from amino acid residue 2 through amino acid residue 23 of gag gene protein p17; or
- 25 (i) a region extending from amino acid residue 89 through amino acid residue 122 of gag gene protein p17.

28. A composition in accordance with claim 19, which further comprises an adjuvant.

29. A composition in accordance with claim 28, wherein said adjuvant comprises a carrier molecule to which the HIV peptide is coupled.

30. A composition in accordance with claim 29, wherein said carrier molecule comprises poly-L-lysine, keyhole limpet hemocyanin, thyroglobulin, an albumin or tetanus toxoid.

31. A composition in accordance with claim 29, wherein said carrier molecule comprises multiple repeats of a glycopeptide.

32. A composition in accordance with claim 31, wherein said carrier molecule comprises multiple repeats of muramyl dipeptide.

33. A composition in accordance with claim 32, wherein said multiple repeats of muramyl dipeptide are crosslinked.

34. A composition in accordance with claim 33, wherein said multiple repeats of muramyl dipeptide comprise a terminal dipeptide of L-alanine-D-isoglutamine.

35. A method of identifying a neutralizing or inactivating region of an HIV protein, wherein said neutralizing or inactivating region does not elicit an immune response in man when encountered by infection or environmental exposure but does elicit an immune response in a non-human mammal, which comprises:

(a) extracting HIV proteins from a lysate of an HIV strain;

(b) immunizing a non-human mammal with said extract;

(c) obtaining antisera from said immunized mammal;

(d) employing said antisera in a competitive immunoassay with human HIV antisera to identify regions of HIV proteins which are recognized by

antibodies in said antisera but not recognized by antibodies in said human antisera; and

(e) determining which of said regions is a neutralizing or inactivating region.

36. A method in accordance with claim 35, wherein said neutralizing or inactivating region comprises or is homologous to one of the following regions of a protein of HIV isolate HIV1<sub>sf2</sub>:

- 5 (a) a region extending from amino acid residue 4 through amino acid residue 27 of gp120;
- (b) a region extending from amino acid residue 54 through amino acid residue 76 of gp120;
- (c) a region extending from amino acid residue 502  
10 through amino acid residue 541 of gp41;
- (d) a region extending from amino acid residue 254 through amino acid residue 295 of reverse transcriptase heterodimer p66/55;
- (e) a region extending from amino acid residue 69  
15 through 94 of protease p10;
- (f) a region extending from amino acid residue 166 through amino acid residue 181 of gag gene protein p24;
- (g) a region extending from amino acid residue 390  
20 through amino acid residue 410 and amino acid residue 438 through 443 of gag gene protein p7;
- (h) a region extending from amino acid residue 2 through amino acid residue 23 of gag gene protein p17; or
- 25 (i) a region extending from amino acid residue 89 through amino acid residue 122 of gag gene protein p17.

37. A method for obtaining antibodies which react with an epitope on a neutralizing or inactivating region of an HIV protein, wherein said neutralizing or inactivating region of said protein fails to elicit an

5 immune response in man when encountered by infection or  
environmental exposure but does elicit an immune  
response in a non-human mammal which comprises:

- (a) isolating proteins from a lysate of an HIV  
isolate;
- 10 (b) identifying an epitope on at least one of said  
proteins which has an amino acid sequence which  
corresponds to or mimics the amino acid sequence  
of a neutralizing or inactivating region which  
15 fails to elicit an immune response in man when  
encountered by infection or environmental exposure  
but does elicit an immune response in a non-human  
mammal;
- (c) combining said proteins with a physiologically  
acceptable carrier;
- 20 (d) immunizing a non-human mammalian host with  
said proteins and carrier; and
- (e) obtaining antibodies to said epitope from said  
immunized host.

38. A method in accordance with claim 37, wherein  
said lysate is treated to remove HLA class I and class  
II antigens.

39. A method in accordance with claim 37, wherein  
said proteins are deglycosylated prior to being  
combined with said physiological carrier.

40. A method in accordance with claim 37, wherein  
the amino acid sequence of said epitope corresponds to  
or mimics a portion of a human protein amino acid  
sequence.

41. A method in accordance with claim 37, wherein  
said protein is conjugated with an adjuvant prior to  
being combined with a physiologically acceptable  
carrier.

42. A method in accordance with claim 41, wherein  
said adjuvant comprises a macromolecular carrier.



43. A method in accordance with claim 42, wherein said macromolecular carrier comprises multiple repeats of muramyl dipeptide.

44. A method in accordance with claim 43, wherein said multiple repeats of muramyl dipeptide comprise a terminal dipeptide of L-alanine-D-isoglutamine.

45. A method in accordance with claim 37, wherein said proteins comprise epitopes which correspond to or mimic more than one neutralizing or inactivating region.

46. A method in accordance with claim 37, wherein said neutralizing or inactivating region comprises a portion of an envelope glycoprotein or transmembrane protein.

47. A method in accordance with claim 45, wherein at least one of said neutralizing or inactivating regions comprises a portion of an envelope glycoprotein or transmembrane protein.

48. A method in accordance with claim 47, which further comprises a neutralizing or inactivating region of protease p10.

49. A method in accordance with claim 37, wherein said epitope corresponds to or mimics an epitope region of HIV1<sub>sf2</sub> which comprises:

- 5 (a) a region extending from amino acid residue 4 through amino acid residue 27 of gp120;
- (b) a region extending from amino acid residue 54 through amino acid residue 76 of gp120;
- (c) a region extending from amino acid residue 502 through amino acid residue 541 of gp41;
- 10 (d) a region extending from amino acid residue 254 through amino acid residue 295 of reverse transcriptase heterodimer p66/55;
- (e) a region extending from amino acid residue 69 through 94 of protease p10;

15 (f) a region extending from amino acid residue 166  
through amino acid residue 181 of gag gene protein  
p24;

(g) a region extending from amino acid residue 390  
through amino acid residue 410 and amino acid  
20 residue 438 through 443 of gag gene protein p7;

(h) a region extending from amino acid residue 2  
through amino acid residue 23 of gag gene protein  
p17; or

(i) a region extending from amino acid residue 89  
25 through amino acid residue 122 of gag gene protein  
p17.

50. A method in accordance with claim 49, wherein  
said proteins comprise epitopes which correspond to or  
mimic more than one neutralizing or inactivating region  
and said epitopes correspond to or mimic two or more of  
5 said epitope regions of HIV<sub>SF2</sub>.

51. A method in accordance with claim 37 or 45,  
wherein said proteins have been enriched for said  
epitope(s).

52. A method in accordance with claim 45, wherein  
said epitopes are present in relative proportions which  
range from about 1:1 to a maximum difference in amount  
between any two epitopes of 10:1.

53. A method for obtaining antibodies which react  
with an epitope on a neutralizing or inactivating  
region of an HIV protein, wherein said neutralizing or  
inactivating region of said protein fails to elicit an  
5 immune response in man when encountered by infection or  
environmental exposure but does elicit an immune  
response in a non-human mammal, which comprises:

(a) synthesizing a peptide having an amino acid  
sequence which corresponds to or mimics an epitope  
10 on a neutralizing or inactivating region of an HIV  
protein, wherein said region fails to elicit an

immune response in man when encountered by  
infection or environmental exposure but does  
elicit an immune response in a non-human mammal;

- 15 (b) combining said peptide with a physiologically  
acceptable carrier;  
(c) immunizing a non-human mammalian host with  
said peptide and carrier; and  
20 (d) obtaining antibodies to said epitope from said  
immunized host.

54. A method in accordance with claim 53, wherein  
said peptide has an amino acid sequence which mimics a  
portion of a human protein amino acid sequence.

55. A method in accordance with claim 53, wherein  
said peptide is conjugated with an adjuvant prior to  
being combined with said physiologically acceptable  
carrier.

56. A method in accordance with claim 55, wherein  
said adjuvant comprises a macromolecular carrier.

57. A method in accordance with claim 56, wherein  
said macromolecular carrier comprises multiple repeats  
of muramyl dipeptide.

58. A method in accordance with claim 57, wherein  
said multiple repeats of muramyl dipeptide comprise a  
terminal dipeptide of L-alanine-D-isoglutamine.

59. A method in accordance with claim 53, which  
comprises a mixture of peptides, each of which has an  
amino acid sequence which corresponds to or mimics an  
epitope on a neutralizing or inactivating region of an  
5 HIV protein, wherein said region fails to elicit an  
immune response in man when encountered by infection or  
environmental exposure but does elicit an immune  
response in a non-human mammal.

60. A method in accordance with claim 53, wherein  
said peptide has an amino acid sequence which  
corresponds to or mimics a neutralizing or inactivating

region which comprises a portion of an envelope  
 5 glycoprotein or transmembrane protein.

61. A method in accordance with claim 59, wherein  
 at least one of peptides has an amino acid sequence  
 which corresponds to or mimics a neutralizing or  
 inactivating region which comprises a portion of an  
 5 envelope glycoprotein or transmembrane protein.

62. A method in accordance with claim 61, which  
 further comprises a peptide which has an amino acid  
 sequence which corresponds to or mimics a neutralizing  
 or inactivating region of protease p10.

63. A method in accordance with claim 53, wherein  
 the amino acid sequence of said peptide corresponds to  
 or mimics the amino acid sequence of an epitope on a  
 neutralizing or inactivating region of a protein of  
 5 HIV1<sub>sf2</sub> which comprises:

(a) a region extending from amino acid residue 4  
 through amino acid residue 27 of gp120;

(b) a region extending from amino acid residue 54  
 through amino acid residue 76 of gp120;

10 (c) a region extending from amino acid residue 502  
 through amino acid residue 541 of gp41;

(d) a region extending from amino acid residue 254  
 through amino acid residue 295 of reverse  
 transcriptase heterodimer p66/55;

15 (e) a region extending from amino acid residue 69  
 through 94 of protease p10;

(f) a region extending from amino acid residue 166  
 through amino acid residue 181 of gag gene protein  
 p24;

20 (g) a region extending from amino acid residue 390  
 through amino acid residue 410 and amino acid  
 residue 438 through 443 of gag gene protein p7;

25 (h) a region extending from amino acid residue 2 through amino acid residue 23 of gag gene protein p17; or

(i) a region extending from amino acid residue 89 through amino acid residue 122 of gag gene protein p17.

64. A method in accordance with claim 59, wherein said peptides correspond to or mimic amino acid sequences of at least two epitopes on neutralizing or inactivating regions of HIV1<sub>sf2</sub> proteins, said regions comprising:

(a) a region extending from amino acid residue 4 through amino acid residue 27 of gp120;

(b) a region extending from amino acid residue 54 through amino acid residue 76 of gp120;

10 (c) a region extending from amino acid residue 502 through amino acid residue 541 of gp41;

(d) a region extending from amino acid residue 254 through amino acid residue 295 of reverse transcriptase heterodimer p66/55;

15 (e) a region extending from amino acid residue 69 through 94 of protease p10;

(f) a region extending from amino acid residue 166 through amino acid residue 181 of gag gene protein p24;

20 (g) a region extending from amino acid residue 390 through amino acid residue 410 and amino acid residue 438 through 443 of gag gene protein p7;

25 (h) a region extending from amino acid residue 2 through amino acid residue 23 of gag gene protein p17; or

(i) a region extending from amino acid residue 89 through amino acid residue 122 of gag gene protein p17.

65. A method in accordance with claim 59, wherein said peptides are present in relative proportions which range from about 1:1 to a maximum difference in amount between any two peptides of 10:1.

5 66. An antibody which recognizes and reacts with an epitope which corresponds to or mimics an epitope on a neutralizing or inactivating region of an HIV protein, wherein said neutralizing or inactivating region of said protein fails to elicit an immune response in man when encountered by infection or environmental exposure.

5 67. An antibody in accordance with claim 66, wherein said epitope has an amino acid sequence which corresponds to or immunologically mimics a portion of a human protein amino acid sequence or a neurotoxin protein amino acid sequence.

68. An antibody in accordance with claim 66, wherein said protein comprises carbohydrate-depleted envelope precursor gp160, gp120 glycoprotein or gp 41 transmembrane glycoprotein.

69. An antibody in accordance with claim 66, wherein said protein comprises a carbohydrate depleted gag precursor p55 or cleaved gag products p17, p24 or p7.

70. An antibody in accordance with claim 66, wherein said protein comprises carbohydrate-depleted protease p10 or reverse transcriptase heterodimer p66/55.

5 71. An antibody in accordance with claim 67, wherein said human protein comprises alpha fetoprotein, aspartyl protease, deoxyuridine 5'-triphosphate nucleotidohydrolase, eosinophil cationic protein or eosinophil-derived neurotoxin.

72. An antibody in accordance with claim 66, wherein said antibody recognizes an epitope which

corresponds to or mimics an epitope on one of the following neutralizing or inactivating regions of HIV isolate HIV1<sub>SF2</sub>:

- (a) a region extending from amino acid residue 4 through amino acid residue 27 of gp120;
- (b) a region extending from amino acid residue 54 through amino acid residue 76 of gp120;
- (c) a region extending from amino acid residue 502 through amino acid residue 541 of gp41;
- (d) a region extending from amino acid residue 254 through amino acid residue 295 of reverse transcriptase heterodimer p66/55;
- (e) a region extending from amino acid residue 69 through 94 of protease p10;
- (f) a region extending from amino acid residue 166 through amino acid residue 181 of gag gene protein p24;
- (g) a region extending from amino acid residue 390 through amino acid residue 410 and amino acid residue 438 through 443 of gag gene protein p7;
- (h) a region extending from amino acid residue 2 through amino acid residue 23 of gag gene protein p17; or
- (i) a region extending from amino acid residue 89 through amino acid residue 122 of gag gene protein p17.

73. A combination of at least two antibodies, each of which recognizes and reacts with an epitope which corresponds to or mimics an epitope on a neutralizing or inactivating region of an HIV protein, wherein said neutralizing or inactivating region of said protein fails to elicit an immune response in man when encountered by infection or environmental exposure.

74. A combination of antibodies in accordance with claim 73, wherein each of said antibodies recognizes and reacts with an epitope which has an amino acid sequence which corresponds to or  
5 immunologically mimics a portion of a human protein amino acid sequence or a neurotoxin protein amino acid sequence.

75. A combination of antibodies in accordance with claim 73, wherein at least one of said antibodies recognizes and reacts with an epitope which corresponds to or mimics an epitope on a neutralizing or  
5 inactivating region of carbohydrate-depleted envelope precursor gp160, gp120 glycoprotein or gp 41 transmembrane glycoprotein.

76. A combination of antibodies in accordance with claim 73, wherein at least one of said antibodies recognizes and reacts with an epitope which corresponds to or mimics an epitope on a neutralizing or  
5 inactivating region of carbohydrate-depleted gag precursor p55 or cleaved gag products p17, p24 or p7.

77. A combination of antibodies in accordance with claim 73, wherein at least one of said antibodies recognizes and reacts with an epitope which corresponds to or mimics an epitope on a neutralizing or  
5 inactivating region of carbohydrate-depleted protease p10 or reverse transcriptase heterodimer p66/55.

78. A combination of antibodies in accordance with claim 74, wherein said human protein comprises alpha fetoprotein, aspartyl protease, deoxyuridine 5'-triphosphate nucleotidohydrolase, eosinophil cationic  
5 protein or eosinophil-derived neurotoxin.

79. A combination of antibodies in accordance with claim 73, wherein at least one of said antibodies recognizes an epitope which corresponds to or mimics an



epitope on one of the following neutralizing or  
 5 inactivating regions of HIV isolate HIV1<sub>SF2</sub>:

- (a) a region extending from amino acid residue 4 through amino acid residue 27 of gp120;
- (b) a region extending from amino acid residue 54 through amino acid residue 76 of gp120;
- 10 (c) a region extending from amino acid residue 502 through amino acid residue 541 of gp41;
- (d) a region extending from amino acid residue 254 through amino acid residue 295 of reverse transcriptase heterodimer p66/55;
- 15 (e) a region extending from amino acid residue 69 through 94 of protease p10;
- (f) a region extending from amino acid residue 166 through amino acid residue 181 of gag gene protein p24;
- 20 (g) a region extending from amino acid residue 390 through amino acid residue 410 and amino acid residue 438 through 443 of gag gene protein p7;
- (h) a region extending from amino acid residue 2 through amino acid residue 23 of gag gene protein p17; or
- 25 (i) a region extending from amino acid residue 89 through amino acid residue 122 of gag gene protein p17.

80. A combination of antibodies in accordance with claim 79, which comprises antibodies which recognize an epitope which corresponds to or mimics an epitope on each of the following neutralizing or  
 5 inactivating regions of HIV isolate HIV1<sub>SF2</sub>:

- (a) a region extending from amino acid residue 4 through amino acid residue 27 of gp120;
- (b) a region extending from amino acid residue 54 through amino acid residue 76 of gp120; and

10 (c) a region extending from amino acid residue 502  
through amino acid residue 541 of gp41.

81. A combination of antibodies in accordance  
with claim 79, which comprises antibodies which  
recognize an epitope which corresponds to or mimics an  
epitope on each of the following neutralizing or  
5 inactivating regions of HIV isolate HIV1<sub>SF2</sub>:

(a) a region extending from amino acid residue 4  
through amino acid residue 27 of gp120;

(b) a region extending from amino acid residue 54  
through amino acid residue 76 of gp120;

10 (c) a region extending from amino acid residue 502  
through amino acid residue 541 of gp41; and

(d) a region extending from amino acid residue 69  
through 94 of protease p10.

82. A combination of antibodies in accordance  
with claim 79, which comprises antibodies which  
recognize epitopes which correspond to or mimic  
epitopes on each of the following neutralizing or  
5 inactivating regions of HIV isolate HIV1<sub>SF2</sub>:

(a) a region extending from amino acid residue 4  
through amino acid residue 27 of gp120;

(b) a region extending from amino acid residue 54  
through amino acid residue 76 of gp120;

10 (c) a region extending from amino acid residue 502  
through amino acid residue 541 of gp41;

and at least one of the following neutralizing or  
inactivating regions of HIV isolate HIV1<sub>SF2</sub>:

(d) a region extending from amino acid residue 69  
15 through 94 of protease p10;

(e) a region extending from amino acid residue 166  
through amino acid residue 181 of gag gene protein  
p24;

20 (f) a region extending from amino acid residue 390 through amino acid residue 410 and amino acid residue 438 through 443 of gag gene protein p7;

(g) a region extending from amino acid residue 2 through amino acid residue 23 of gag gene protein p17; or

25 (h) a region extending from amino acid residue 89 through amino acid residue 122 of gag gene protein p17

(i) a region extending from amino acid residue 254 through 295 of reverse transcriptase heterodimer p66/55.

30 83. A combination of antibodies in accordance with claim 73, wherein said antibodies recognize epitopes which corresponds to or mimic epitopes on the following neutralizing or inactivating regions of HIV isolate HIV1<sub>sf2</sub>:

(a) a region extending from amino acid residue 4 through amino acid residue 27 of gp120;

(b) a region extending from amino acid residue 54 through amino acid residue 76 of gp120;

10 (c) a region extending from amino acid residue 502 through amino acid residue 541 of gp41;

(d) a region extending from amino acid residue 254 through amino acid residue 295 of reverse transcriptase heterodimer p66/55;

15 (e) a region extending from amino acid residue 69 through 94 of protease p10;

(f) a region extending from amino acid residue 166 through amino acid residue 181 of gag gene protein p24;

20 (g) a region extending from amino acid residue 390 through amino acid residue 410 and amino acid residue 438 through 443 of gag gene protein p7;

25

(h) a region extending from amino acid residue 2 through amino acid residue 23 of gag gene protein p17; and

(i) a region extending from amino acid residue 89 through amino acid residue 122 of gag gene protein p17.

84. A composition comprising a combination of antibodies in accordance with claim 79 in a pharmaceutically acceptable carrier.

85. A composition comprising a combination of antibodies in accordance with claim 80 in a pharmaceutically acceptable carrier.

86. A composition comprising a combination of antibodies in accordance with claim 81 in a pharmaceutically acceptable carrier.

87. A composition comprising a combination of antibodies in accordance with claim 82 in a pharmaceutically acceptable carrier.

88. A composition comprising a combination of antibodies in accordance with claim 83 in a pharmaceutically acceptable carrier.

89. An antibody in accordance with claim 66, which is bound to a toxin or a radioactive material.

90. An antibody in accordance with claim 66, which is aggregated with a human T-cell activator.

91. A composition comprising an antibody in accordance with claim 66 in combination with aside-3'deoxythymidine, 2',3'-dideoxycytidine, 2',3'-dideoxy-2',3'-didehydrocytidine.

92. A composition comprising the proteins of claim 1 in combination with a pharmaceutically acceptable carrier.

93. A composition in accordance with claim 92, wherein said proteins are coupled to a macromolecular carrier.

94. A composition in accordance with claim 93, wherein said carrier is a microparticle of muramyl dipeptide.

95. A composition comprising one or more synthetic peptides of claim 19 in combination with a pharmaceutically acceptable carrier.

96. a composition in accordance with claim 95, wherein said peptides are coupled to a macromolecular carrier.

97. A composition in accordance with claim 96, wherein said carrier is a microparticle of muramyl dipeptide.

98. A method of inhibiting an infection of HIV in a human infected with the virus which comprises administering to said patient a therapeutically effective amount of a composition comprising one or more antibodies each of which recognizes and reacts with an epitope which corresponds to or mimics an epitope on a neutralizing or inactivating region of an HIV protein, wherein said neutralizing or inactivating region of said protein fails to elicit an immune response in man.

99. A method in accordance with claim 98, wherein said epitope has an amino acid sequence which corresponds to or immunologically mimics a portion of a human protein amino acid sequence when encountered by infection or environmental exposure.

100. A method in accordance with claim 98, wherein said protein comprises carbohydrate-depleted envelope precursor gp160, gp 120 glycoprotein or gp 41 transmembrane.

101. A method in accordance with claim 99, wherein said protein comprises carbohydrate-depleted gag precursor p55 or cleaved gag products p17, p24 or p7.

102. A method in accordance with claim 98, wherein said protein comprises carbohydrate-depleted protease p10 or reverse transcriptase heterodimer p66/55.

103. A method in accordance with claim 98, wherein said antibody is administered at a daily dose of about 0.1 to about 200 mg per kilogram of body weight.

104. A method in accordance with claim 98, wherein a combination of antibodies is administered and the ratio of each of said antibodies to one another does not differ by more than a factor of 10.

105. A method in accordance with claim 104, wherein the ratio of each of said antibodies to one another is approximately 1:1.

106. A method in accordance with claim 98 wherein said antibodies are conjugated to a macromolecular carrier.

107. A method in accordance with claim 106 wherein said carrier is a muramyl dipeptide microparticle.

108. A method in accordance with claim 98, wherein said antibody recognizes an epitope which corresponds to or mimics an epitope on one of the following neutralizing or inactivating regions of HIV isolate HIV1<sub>sf2</sub>:

(a) a region extending from amino acid residue 4 through amino acid residue 27 of gp120;

(b) a region extending from amino acid residue 54 through amino acid residue 76 of gp120;

(c) a region extending from amino acid residue 502 through amino acid residue 541 of gp41;

(d) a region extending from amino acid residue 254 through amino acid residue 295 of reverse transcriptase heterodimer p66/55;

- 15 (e) a region extending from amino acid residue 69  
through 94 of protease p10;  
(f) a region extending from amino acid residue 166  
through amino acid residue 181 of gag gene protein  
p24;
- 20 (g) a region extending from amino acid residue 390  
through amino acid residue 410 and amino acid  
residue 438 through 443 of gag gene protein p7;  
(h) a region extending from amino acid residue 2  
through amino acid residue 23 of gag gene protein  
p17; or
- 25 (i) a region extending from amino acid residue 89  
through amino acid residue 122 of gag gene protein  
p17.

109. A method in accordance with claim 108,  
wherein at least two antibodies are administered and  
each of said antibodies recognizes and reacts with an  
epitope which corresponds to or mimics an epitope on a  
neutralizing or inactivating region of an HIV protein,  
5 wherein said neutralizing or inactivating region of  
said protein fails to elicit an immune response in man  
when encountered by infection or environmental  
exposure.

110. A method in accordance with claim 109,  
wherein at least one of said antibodies recognizes and  
reacts with an epitope which corresponds to or mimics  
an epitope on a neutralizing or inactivating region of  
5 carbohydrate-depleted envelope precursor gp160, gp120  
glycoprotein or gp41 transmembrane.

111. A method in accordance with claim 109,  
wherein at least one of said antibodies recognizes and  
reacts with an epitope which corresponds to or mimics  
an epitope on a neutralizing or inactivating region of  
5 carbohydrate-depleted gag precursor p55 or cleaved gag  
products p17, p24 or p7.

112. A method in accordance with claim 109,  
wherein at least one of said antibodies recognizes and  
reacts with an epitope which corresponds to or mimics  
an epitope on a neutralizing or inactivating region of  
5 carbohydrate-depleted protease p10 or reverse  
transcriptase heterodimer p66/55.

113. A method in accordance with claim 109, which  
comprises antibodies which recognize and react with  
epitopes which correspond to or mimic epitopes from  
each of the following neutralizing or inactivating  
5 regions of HIV isolate HIV<sub>1SF2</sub>:

- (a) a region extending from amino acid residue 4  
through amino acid residue 27 of gp120;
- (b) a region extending from amino acid residue 54  
through amino acid residue 76 of gp120;
- 10 (c) a region extending from amino acid residue 502  
through amino acid residue 541 of gp41;
- (d) a region extending from amino acid residue 254  
through amino acid residue 295 of reverse  
transcriptase heterodimer p66/55;
- 15 (e) a region extending from amino acid residue 69  
through 94 of protease p10;
- (f) a region extending from amino acid residue 166  
through amino acid residue 181 of gag gene protein  
p24;
- 20 (g) a region extending from amino acid residue 390  
through amino acid residue 410 and amino acid  
residue 438 through 443 of gag gene protein p7;
- (h) a region extending from amino acid residue 2  
through amino acid residue 23 of gag gene protein  
25 p17; or
- (i) a region extending from amino acid residue 89  
through amino acid residue 122 of gag gene protein  
p17.



114. A method for neutralizing or inactivating one or more essential steps in the life cycle of HIV in a patient infected with the virus which comprises administering to said patient a therapeutically  
5 effective amount of a composition comprising one or more antibodies each of which recognizes and reacts with an epitope which corresponds to or mimics an epitope on a neutralizing or inactivating region of an HIV protein, wherein said neutralizing or inactivating  
10 region of said protein fails to elicit an immune response in man.

115. A method in accordance with claim 112, wherein said epitope has an amino acid sequence which corresponds to or immunologically mimics a portion of a human protein amino acid sequence.

116. A method in accordance with claim 114, wherein said antibody recognizes an epitope which corresponds to or mimics an epitope on one of the following neutralizing or inactivating regions of HIV  
5 isolate HIV1<sub>SF2</sub>:

(a) a region extending from amino acid residue 4 through amino acid residue 27 of gp120;

(b) a region extending from amino acid residue 54 through amino acid residue 76 of gp120;

10 (c) a region extending from amino acid residue 502 through amino acid residue 541 of gp41;

(d) a region extending from amino acid residue 254 through amino acid residue 295 of reverse transcriptase heterodimer p66/55;

15 (e) a region extending from amino acid residue 69 through 94 of protease p10;

(f) a region extending from amino acid residue 166 through amino acid residue 181 of gag gene protein p24;

- 20 (g) a region extending from amino acid residue 390  
through amino acid residue 410 and amino acid  
residue 438 through 443 of gag gene protein p7;  
(h) a region extending from amino acid residue 2  
through amino acid residue 23 of gag gene protein  
25 p17; or  
(i) a region extending from amino acid residue 89  
through amino acid residue 122 of gag gene protein  
p17.

117. A method in accordance with claim 115,  
wherein at least two antibodies are administered and  
each of said antibodies recognizes and reacts with an  
epitope which corresponds to or mimics an epitope on a  
5 neutralizing or inactivating region of an HIV protein,  
wherein said neutralizing or inactivating region of  
said protein fails to elicit an immune response in man.

118. A method in accordance with claim 114, which  
comprises antibodies which recognize and react with  
epitopes which correspond to or mimic epitopes from  
each of the following neutralizing or inactivating  
5 regions of HIV isolate HIV1<sub>SF2</sub>:

- (a) a region extending from amino acid residue 4  
through amino acid residue 27 of gp120;  
(b) a region extending from amino acid residue 54  
through amino acid residue 76 of gp120; and  
10 (c) a region extending from amino acid residue 502  
through amino acid residue 541 of gp41.

119. A method in accordance with claim 114, which  
comprises antibodies which recognize and react with  
epitopes which correspond to or mimic epitopes from  
each of the following neutralizing or inactivating  
5 regions of HIV isolate HIV1<sub>SF2</sub>:

- (a) a region extending from amino acid residue 4  
through amino acid residue 27 of gp120;

(b) a region extending from amino acid residue 54 through amino acid residue 76 of gp120;

10 (c) a region extending from amino acid residue 502 through amino acid residue 541 of gp41; and

(d) a region extending from amino acid residue 69 through 94 of protease p10.

120. A method in accordance with claim 114, which comprises antibodies which recognize and react with epitopes which correspond to or mimic epitopes from each of the following neutralizing or inactivating  
5 regions of HIV isolate HIV1<sub>SF2</sub>:

(a) a region extending from amino acid residue 4 through amino acid residue 27 of gp120;

(b) a region extending from amino acid residue 54 through amino acid residue 76 of gp120;

10 (c) a region extending from amino acid residue 502 through amino acid residue 541 of gp41;

(d) a region extending from amino acid residue 254 through amino acid residue 295 of reverse transcriptase heterodimer p66/55;

15 (e) a region extending from amino acid residue 69 through 94 of protease p10;

(f) a region extending from amino acid residue 166 through amino acid residue 181 of gag gene protein p24;

20 (g) a region extending from amino acid residue 390 through amino acid residue 410 and amino acid residue 438 through 443 of gag gene protein p7;

(h) a region extending from amino acid residue 2 through amino acid residue 23 of gag gene protein p17; or  
25

(i) a region extending from amino acid residue 89 through amino acid residue 122 of gag gene protein p17.

121. A method in accordance with claim 114, wherein said antibodies are conjugated to a macromolecular carrier.

122. A method in accordance with claim 121, wherein said carrier comprises a muramyl dipeptide microparticle.

123. A method for preventing HIV infection in a patient who has been exposed to HIV which comprises administering to said patient a therapeutically effective amount of a composition comprising one or more antibodies each of which recognizes and reacts with an epitope which corresponds to or mimics an epitope on a neutralizing or inactivating region of an HIV protein, wherein said neutralizing or inactivating region of said protein fails to elicit an immune response in man when encountered by infection or environmental exposure.

124. A method in accordance with claim 119, wherein said epitope has an amino acid sequence which corresponds to or immunologically mimics a portion of a human protein amino acid sequence.

125. A method in accordance with claim 119, wherein said antibody recognizes an epitope which corresponds to or mimics an epitope on one of the following neutralizing or inactivating regions of HIV isolate HIV1<sub>RT</sub>:

- (a) a region extending from amino acid residue 4 through amino acid residue 27 of gp120;
- (b) a region extending from amino acid residue 54 through amino acid residue 76 of gp120;
- (c) a region extending from amino acid residue 502 through amino acid residue 541 of gp41;
- (d) a region extending from amino acid residue 254 through amino acid residue 295 of reverse transcriptase heterodimer p66/55;

- 15 (e) a region extending from amino acid residue 69 through 94 of protease p10;
- (f) a region extending from amino acid residue 166 through amino acid residue 181 of gag gene protein p24;
- 20 (g) a region extending from amino acid residue 390 through amino acid residue 410 and amino acid residue 438 through 443 of gag gene protein p7;
- (h) a region extending from amino acid residue 2 through amino acid residue 23 of gag gene protein p17; or
- 25 (i) a region extending from amino acid residue 89 through amino acid residue 122 of gag gene protein p17.

126. A method in accordance with claim 125, wherein at least two antibodies are administered and each of said antibodies recognizes and reacts with an epitope which corresponds to or mimics an epitope on a neutralizing or inactivating region of an HIV protein, wherein said neutralizing or inactivating region of said protein fails to elicit an immune response in man.

127. A method in accordance with claim 125, which comprises antibodies which recognize and react with epitopes which correspond to or mimic epitopes from each of the following neutralizing or inactivating regions of HIV isolate HIV1<sub>sf2</sub>:

- (a) a region extending from amino acid residue 4 through amino acid residue 27 of gp120;
- (b) a region extending from amino acid residue 54 through amino acid residue 76 of gp120; and
- 10 (c) a region extending from amino acid residue 502 through amino acid residue 541 of gp41.

128. A method in accordance with claim 125, which comprises antibodies which recognize and react with epitopes which correspond to or mimic epitopes

from each of the following neutralizing or inactivating  
 5 regions of HIV isolate HIV1<sub>SF2</sub>:

- (a) a region extending from amino acid residue 4  
 through amino acid residue 27 of gp120;
- (b) a region extending from amino acid residue 54  
 through amino acid residue 76 of gp120;
- 10 (c) a region extending from amino acid residue 502  
 through amino acid residue 541 of gp41; and
- (d) a region extending from amino acid residue 69  
 through 94 of protease p10.

129. A method in accordance with claim 125, which  
 comprises antibodies which recognize and react with  
 epitopes which correspond to or mimic epitopes from  
 each of the following neutralizing or inactivating

5 regions of HIV isolate HIV1<sub>SF2</sub>:

- (a) a region extending from amino acid residue 4  
 through amino acid residue 27 of gp120;
- (b) a region extending from amino acid residue 54  
 through amino acid residue 76 of gp120;
- 10 (c) a region extending from amino acid residue 502  
 through amino acid residue 541 of gp41;
- (d) a region extending from amino acid residue 254  
 through amino acid residue 295 of reverse  
 transcriptase heterodimer p66/55;
- 15 (e) a region extending from amino acid residue 69  
 through 94 of protease p10;
- (f) a region extending from amino acid residue 166  
 through amino acid residue 181 of gag gene protein  
 p24;
- 20 (g) a region extending from amino acid residue 390  
 through amino acid residue 410 and amino acid  
 residue 438 through 443 of gag gene protein p7;
- (h) a region extending from amino acid residue 2  
 through amino acid residue 23 of gag gene protein  
 25 p17; or

(i) a region extending from amino acid residue 89 through amino acid residue 122 of gag gene protein p17.

130. A method for detecting the presence of HIV in a biological fluid sample from an individual who may have been infected with HIV which comprises employing an antibody of claim 66 in an antibody-antigen assay in which said antibody is combined with a sample of body fluid from said individual under conditions conducive to antibody-antigen complex formation and determining whether said antibody binds to an HIV antigen.

131. A method for detecting the presence of HIV in an individual who may have been infected with HIV which comprises employing an antibody of claim 66 in an enzyme immunoassay, wherein said antibody is conjugated to an enzyme and contacted with a sample of body fluid from said individual under conditions conducive to antibody-antigen complex formation and determining whether said antibody binds to an HIV antigen.

132. A method for purifying protein containing at least one epitope which corresponds to or mimics an epitope of a neutralizing or inactivating region of an HIV protein from a protein solution, which comprises immobilizing an antibody in accordance with claim 66 to a substrate or solid support, contacting said immobilized antibody with a solution containing said protein under conditions suitable for the formation of immune complexes between said antibody and said protein, separating unbound protein from protein bound to said antibody, and releasing said bound protein from said antibody and recovering said protein.

133. A composition comprising viral proteins isolated from a viral lysate which has been treated to remove human HLA class I and class II antigens present in said lysate, wherein said proteins have been

5 deglycosylated and wherein said proteins comprise at  
least one epitope region which does not elicit an  
immune response in man when encountered through  
infection environmental exposure but does elicit an  
immune response in at least one non-human mammalian  
10 species.

134. A composition in accordance with claim 133,  
wherein said epitope region encompasses a neutralizing  
or inactivating region of said viral protein.

135. A composition in accordance with claim 133,  
wherein said epitope region has an amino acid sequence  
which corresponds to or immunologically mimics a  
portion of a human protein amino acid sequence.

136. A composition in accordance with claim 133,  
wherein said proteins are coupled to a macromolecular  
carrier.

137. A composition in accordance with claim 136,  
wherein said carrier is a muramyl dipeptide  
microparticle.

138. A composition in accordance with claim 136,  
wherein said muramyl dipeptide comprises a terminal  
dipeptide of L-alanine-D-isoglutamine.

139. A composition comprising a synthetic peptide  
which comprises an epitope region which corresponds to  
or mimics a neutralizing or inactivating region of a  
viral protein, wherein said peptide does not elicit an  
5 immune response in humans when encountered through  
infection or environmental exposure but does elicit an  
immune response in at least one non-human mammal.

140. A composition in accordance with claim 139,  
wherein said epitope region has an amino acid sequence  
which corresponds to or immunologically mimics a  
portion of a human protein amino acid sequence.



141. A composition in accordance with claim 139, wherein said proteins are coupled to a macromolecular carrier.

142. A composition in accordance with claim 141, wherein said carrier is a muramyl dipeptide microparticle.

143. A composition in accordance with claim 141, wherein said muramyl dipeptide comprises a terminal dipeptide of L-alanine-D-isoglutamine.

144. A method for identifying a neutralizing or inactivating region of a viral protein, wherein said neutralizing or inactivating region does not elicit an immune response in man when encountered through  
5 infection or environmental exposure but does elicit an immune response in a non-human animal, which comprises:

(a) extracting viral proteins from a viral lysate;  
(b) immunizing a non-human mammal with said extract;

10 (c) obtaining antisera from said immunized mammal;  
(d) employing said antisera in a competitive immunoassay with human viral antisera to identify regions of viral proteins which are recognized by antibodies in said ... sera but not recognized by  
15 antibodies in said human sera; and

(e) determining which of said regions is a neutralizing or inactivating region.

145. A method for obtaining antibodies which react with an epitope on a neutralizing or inactivating region of a protein, wherein said neutralizing or inactivating region of said protein fails to elicit an  
5 immune response in man when encountered through infection or environmental exposure but does elicit an immune response in a non-human mammal which comprises:

(a) isolating proteins from a viral lysate;

- 10 (b) identifying an epitope on at least one of said proteins which has an amino acid sequence which corresponds to or mimics the amino acid sequence of a neutralizing or inactivating region which fails to elicit an immune response in man but does elicit an immune response in a non-human mammal;
- 15 (c) combining said proteins with a physiologically acceptable carrier;
- (d) immunizing a non-human mammalian host with said proteins and carrier; and
- 20 (e) obtaining antibodies to said epitope from said immunized host.

146. A method in accordance with claim 145, wherein said proteins are treated to remove HLA class I and class I antigens and to remove carbohydrates prior to being combined with said physiological carrier.

147. A method in accordance with claim 146, wherein said proteins are conjugated to a macromolecular carrier comprising a muramyl dipeptide microparticle prior to being combined with said physiological carrier.

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148. A method for obtaining antibodies which react with an epitope on a neutralizing or inactivating region of a viral protein, wherein said neutralizing or inactivating region of said protein fails to elicit an immune response in man when encountered through infection or environmental exposure but does elicit an immune response in a non-human mammal, which comprises:

5

(a) synthesizing a peptide having an amino acid sequence which corresponds to or mimics an epitope on a neutralizing or inactivating region of a viral protein, wherein said region fails to elicit an immune response in man but does elicit an immune response in a non-human mammal;

10

- 15 (b) combining said peptide with a physiologically acceptable carrier;
- (c) immunizing a non-human mammalian host with said peptide and carrier; and
- (d) obtaining antibodies to said epitope from said immunized host.

149. A method in accordance with claim 148, wherein said proteins are treated to remove HLA class I and class I antigens and to remove carbohydrates prior to being combined with said physiological carrier.

150. A method in accordance with claim 149, wherein said proteins are conjugated to a macromolecular carrier comprising a muramyl dipeptide microparticle prior to being combined with said physiological carrier.

5

151. An antibody which recognizes and reacts with an epitope which corresponds to or mimics an epitope on a neutralizing or inactivating region of a viral protein, wherein said neutralizing or inactivating region of said protein fails to elicit an immune response in man when encountered through infection or the environmental exposure.

5

152. A combination of at least two antibodies, each of which recognizes and reacts with an epitope which corresponds to or mimics an epitope on a neutralizing or inactivating region of a viral protein, wherein said neutralizing or inactivating region of said protein fails to elicit an immune response in man when encountered through infection or environmental exposure.

5

153. A method of inhibiting a viral infection in a human infected with the virus which comprises administering to said patient a therapeutically effective amount of a composition comprising one or more antibodies each of which recognizes and reacts

5

with an epitope which corresponds to or mimics an epitope on a neutralizing or inactivating region of a protein of the virus, wherein said neutralizing or inactivating region of said protein fails to elicit an immune response in man when encountered through infection or environmental exposure.

154. A method in accordance with claim 153, wherein said antibodies are conjugated to muramyl dipeptide microparticles.

155. A method for preventing a viral infection in a patient who has been exposed to the virus which comprises administering to said patient a therapeutically effective amount of a composition comprising one or more antibodies each of which recognizes and reacts with an epitope which corresponds to or mimics an epitope on a neutralizing or inactivating region of an HIV protein, wherein said neutralizing or inactivating region of said protein fails to elicit an immune response in man when encountered through infection or environmental exposure.

156. A method for detecting the presence of a virus in a biological fluid sample from an individual who may have been infected with the virus which comprises employing an antibody of claim 150 in an antibody-antigen assay in which said antibody is combined with a sample of body fluid from said individual under conditions conducive to antibody-antigen complex formation and determining whether said antibody binds to an antigen of the virus.

157. A method for detecting the presence of a virus in an individual who may have been infected with the virus which comprises employing an antibody of claim 151 in an enzyme immunoassay, wherein said antibody is conjugated to an enzyme and contacted with

a sample of body fluid from said individual under conditions conducive to antibody-antigen complex formation and determining whether said antibody binds to an antigen of the virus.

158. A method for purifying protein containing at least one epitope which corresponds to or mimics an epitope of a neutralizing or inactivating region of a viral protein from a protein solution, which comprises  
5 immobilizing an antibody in accordance with claim 150 to a substrate or solid support, contacting said immobilized antibody with a solution containing said protein under conditions suitable for the formation of immune complexes between said antibody and said  
10 protein, separating unbound protein from protein bound to said antibody, and releasing said bound protein from said antibody and recovering said protein.